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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,222	FERGUSON ET AL.	
	Examiner	Art Unit	
	SATYANARAYANA R. GUDIBANDE	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7, 9-11 and 15-22* is/are pending in the application.

4a) Of the above claim(s) *6,7,9-11 and 15-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of group I invention (claims 1-7 and 12-14) without traverse in the reply filed on 4/16/07 was acknowledged and the applicants request to include claims 8-11 for examination was granted in the office action dated 6/22/07. Applicant's election of pulmonary fibrosis and decanoyl-RVKR as species with traverse was acknowledged, and traversal arguments were answered in the office action dated 6/22/07.

Newly submitted claims 18-22 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the scope of the newly submitted claims do not commensurate with the scope of the original invention elected for examination. The new claims recite a limitation "preventing or inhibiting" which is broader in scope compared to the limitation "reducing" recited in the originally elected invention. Thus the newly submitted claims do not further limit the scope of the base claim. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 18-22 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's amendment to claims in the response filed on 12/21/07 has been acknowledged.

Claims 1-7, 9-11 and 15-22 are pending.

Claims 6, 7 and 9-11 have been withdrawn from further consideration as being drawn to non-elected species.

Claims 15-22 have been withdrawn from further consideration as being drawn to non-elected invention.

Claims 1-5 are examined on the merit.

Any objections and rejections made in the previous office action dated 6/22/07 not specifically mentioned here are considered withdrawn.

Applicants have canceled subject matter related to elected species of pulmonary fibrosis in the in the genus of fibrotic disorder.

Withdrawn Rejections

Claim Rejections - 35 USC § 112 first paragraph: Enablement

Applicant's arguments, see pages 6 and 7, filed 12/21/07, with respect to enablement rejection under 35 USC 112, first paragraph have been fully considered and are persuasive. The rejection of claims 1-4 has been withdrawn in view of amendments to the claims.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 remain rejected under 35 USC 102(b) as being anticipated by Canadian patent application CA 2312109 of Dubois, as stated for claims 1-3, 8 and 12-14 in the previous office action dated 6/22/07 and reiterated below in the modified form to meet the limitations of claims as amended. Please note that response to argument follows the reiterated rejection.

In the instant application, applicants claim a method for **"reducing the normal scarring response"** during the healing of wounds, comprising applying a furin inhibitor to a site of a wound, wherein said furin inhibitor inhibits TGF-β activation.

Dubois discloses a protein-based protease inhibitor that is a mutant of serpin α1-antitripsin wherein the reactive site has Arg-Ile-Pro-Arg^{358} sequence (known as PDX). This mutant has been shown to be a potent furin inhibitor (page 5, paragraph 2). The reference also discloses PDX or a construct, variant, analog, peptide, peptidomimetic, salt and derivatives thereof in the preparation of pharmaceutical compositions for the inhibition of furin or furin-like protease activity in inflammatory and abnormal wound healing and arthritis and others (Page 8, paragraph 2). Furin or furin-like protease activity includes the activity of proprotein convertases such as PACE4, PC%/6 or PC7 (page 8, paragraphs 1 and 2). This meets the limitations of claims 1 and 2. The reference also discloses pharmaceutical composition of that includes compositions with viscous paraffin, fatty acid mono and diglycerides (page 13, paragraph 1) and use of non-aqueous vehicles such as cottonseed oil and other oils (page 14, paragraph 1) that are

useful in solubilizing lipid soluble active agents. This meets the limitations of claim 3. The cited reference teaches the use of PDX or a construct, variant, analog, peptide, peptidomimetic, salt complex derivative thereof for abnormal wound healing with furin or furin-like inhibitors, therefore, it inherently reduces **normal scarring response** during healing of wounds (page 8, paragraphs 1 and 2). Therefore, the claims 1-3 of instant application are anticipated by the cited reference of Dubois.

Response to arguments

Applicants argue that, the scarring resulting from a fibrotic disorder is not encompassed by the currently claimed methods and the instant method relates to the treatment of scarring that is not related to a fibrotic disorder or condition, i.e., normal scarring. Applicants further state that the cited reference discloses pulmonary fibrosis and abnormal wound healing that are exemplary "erosive diseases" in abnormal wound healing erosive disease results in a continuous degradation of extracellular matrix to form a chronic, **non-healing** (abnormal) **wound**. In contrast, the normal scarring process involves an accumulation of extracellular matrix components at a site of injury that does not result or involve a fibrotic condition. The cited reference of Dubois is silent regarding the use of furin inhibitors to reduce, inhibit or prevent normal scarring that specifically inhibit TGF-β activation.

Applicant's arguments filed 12/21/07 have been fully considered but they are not persuasive. It should be noted that the applicant's claim is drawn to a method comprising of applying a furin inhibitor to a site of wound for reducing "the normal scarring response" during

wound healing. The claim as recited does not imply that the method is for "reducing normal scarring". The claim as recited is a method for "reducing normal scarring **response**" during the healing of **wounds**. More over, the instant specification as filed fails to provide a proper definition for the "normal scarring response". The active method step for the claimed invention is the application of a furin inhibitor to the wound site. The claim as recited does not recite "normal" or "abnormal wounds" but recites wounds in general. The reference of Dubois teaches such a method of applying furin inhibitor to the site of wound. The cited reference discloses a furin inhibitor. Since the reference teaches a furin inhibitor, it is inherent that the furin inhibitor inhibits TGF-β activation, because, the claim as recited is drawn to a genus of furin inhibitors.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4 and 5 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dubois as applied to claims 1-3 above, and further in view of Pearton, et al., 2001, Exp Dermatology, 10, 193-203, as stated previous office action dated 6/22/07 and reiterated below in the modified form to meet the limitations of claims as amended. Please note that response to argument follows the reiterated rejection.

In the instant application, applicants claim a method for **"reducing the normal scarring response"** during the healing of wounds, comprising applying a furin inhibitor to a site of a wound, wherein said furin inhibitor inhibits TGF-β activation.

Dubois discloses a protein-based protease inhibitor that is a mutant of serpin α1-antitripsin wherein the reactive site has Arg-Ile-Pro-Arg^{358} sequence (known as PDX). This mutant has been shown to be a potent furin inhibitor (page 5, paragraph 2). The reference also discloses PDX or a construct, variant, analog, peptide, peptidomimetic, salt and derivatives thereof in the preparation of pharmaceutical compositions for the inhibition of furin or furin-like protease activity in inflammatory and abnormal wound healing and arthritis and others (Page 8, paragraph 2). Furin or furin-like protease activity includes the activity of proprotein convertases such as PACE4, PC%/6 or PC7 (page 8, paragraphs 1 and 2). This meets the limitations of claims 1 and 2. The reference also discloses pharmaceutical composition of that includes compositions with viscous paraffin, fatty acid mono and diglycerides (page 13, paragraph 1) and use of non-aqueous vehicles such as cottonseed oil and other oils (page 14, paragraph 1) that are useful in solubilizing lipid soluble active agents. This meets the limitations of claim 3. The cited reference teaches the use of PDX or a construct, variant, analog, peptide, peptidomimetic, salt

complex derivative thereof for abnormal wound healing with furin or furin-like inhibitors, therefore, it inherently reduces **normal scarring response** during healing of wounds (page 8, paragraphs 1 and 2).

Although, the reference of Dubois discloses PDX or a construct, variant, analog, peptide, peptidomimetic, salt and derivatives thereof in the preparation of pharmaceutical compositions for the inhibition of furin or furin-like protease activity, it does not specifically disclose the elected species decanoyl-RVKR-cmk.

Pearton, et al., discloses the elected species decanoyl-RVKR-cmk. The cited reference of Pearton teaches that the decanoyl-RVKR-cmk as a peptide PC inhibitor inhibits the cleavage of Notch-1, a receptor important in cell fate determination and is found throughout the epidermis (Abstract). The decanoyl-RVKR-cmk is a chloromethylketone peptide. The reference teaches that a protease family that has been implicated in processing and differentiation in a number of tissues is the Proprotein Convertase (PC) family. Furin (also known as PACE), PACE4, PC5/6 or PC7/8 belongs to this proprotein Convertase (PC) family. The PC enzymes recognize basic motifs, cleaving after paired basic residues (PC2 and PC1/3) or after a canonical RX(R/K)R motif (furin and PACE4). Furin has been shown to process a wide variety of substrates including receptors, growth factors, hormones, plasma proteins, matrix metalloproteinases and extracellular matrix components. Several proteins relevant to keratinocyte development have been shown to be substrates for PC processing or contain potential PC cleavage sites that include receptors such as Notch-1 receptors (page 193 column 2, and 194 column 1). Pearton, et al., tested the inhibition of furin with decanoyl-RVKR-cmk in the processing of Notch-1 receptor that has a key role in the cell fate determination and patterning. The inhibition of the processing

of Notch-1 from the precursor form (220kDa) to the functional 120 kDa was observed indicating the inhibition of the furin, which is a proprotein Convertase (page 199, column 2, paragraph 2). The fact that decanoyl-RVKR-cmk is a peptide choromethylketone and inhibits furin, which is a proprotein Convertase meets, the limitations of claims 4 and 5. The reference of Pearton teaches that the Decanoyl-RVKR-CMK is a **cell permeable** PC inhibitor (page 199, column 2, paragraph 2).

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Dubois and Pearton, et al., in order to develop a method for reducing scarring during the healing of wounds, reducing fibrosis in the treatment of fibrotic conditions, or for preventing or inhibiting scar formation or fibrosis, comprising applying a furin inhibitor to a site of a wound or fibrotic disorder. Because, Dubois teaches the composition of protein based protease inhibitors for furin and furin-like activity and Pearton teaches that decanoyl-RVKR-cmk inhibits the activity of furin a PC enzyme. The motivation comes from the fact that Dubois teaches use of PDX or a construct, **variant, analog, peptide, peptidomimetic, salt and derivatives thereof** in the preparation of pharmaceutical compositions for the inhibition of furin or furin-like protease activity in inflammatory and erosive diseases that includes pulmonary fibrosis, abnormal wound healing and arthritis and others and Pearton teaches that decanoyl-RVKR-cmk is a peptide choromethylketone and inhibits furin which is a proprotein Convertase that inhibits the processing of Notch-1 receptor that is involved in the cell fate determination and patterning of epidermis. Also, that the Decanoyl-RVKR-CMK is a **cell permeable** PC inhibitor. Cited reference of Pearton also teaches that proprotein convertases (PCs) may play multiple roles during the differentiation of cells within the epidermis (page 202, column 1, paragraph 2). There

would have been reasonable expectation of success given the fact that Dubois taught that analogs, peptides and peptide mimetics of PDX could be used in formulations for the inhibition of furin or furin-like protease activity and the fact that the elected species of the instant invention was used in the inhibition of furin to inhibit the processing of Notch-1 receptor that is key in the cell fate determination and patterning of epidermis. The fact the Decanoyl-RVKR-CMK is a **cell permeable** PC inhibitor, one would have reasonable expectation to use this analog of the furin inhibitor as it has been shown to be a good cell permeation property compared to other analogs, variants, salts or derivatives thereof.

Therefore, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to applicant's argument

Applicants argue that the cited combination of Dubois and Pearton fail to render the claimed methods prima facie obvious. As discussed above, Dubois fails to teach or suggest the use of furin inhibitors in reduction, treatment or prevention of normal scarring during wound healing. Pearton fails to correct this deficiency as it discloses only that decanoyl-RVKR- cmk appears to play a role in differentiation of keratinocytes in the epidermis. Thus, the cited combination of references fails to teach each and every element of the claimed methods.

Applicants further argue that a person of ordinary skill in the art would find no motivation or common sense basis to support combining the disclosures of these references to result in the claimed methods. Applicants state that, "Dubois describes chronic conditions, in which the prolonged influence of cytokines on the inflammatory response eventually gives rise

to a disease state in which extracelluar matrix is degraded and tissue structure compromised. This is quite distinct from the normal scarring response to wounding of the claimed methods, where acute action of cytokines (including, e.g., TGF-β1 and TGF-β2 released as a sudden bolus from de-granulating platelets) establishes a local milieu in which cells are stimulated to deposit extracellular matrix. Thus, Dubois appears to suggest that furin inhibitors (such as PDX) may be of benefit in the treatment of chronic conditions over a protracted period of time. Pearton fails to provide any additional motivation that would suggest using furin inhibitors to inhibit the normal scarring response in the absence of a fibrotic condition as Pearton focuses exclusively on the activity of a single furin inhibitor on terminal differentiation of keratinocytes in the skin. Applicants note that the allegedly shared cell permeability feature would not be enough to inform a person of ordinary skill in the art to use the inhibitor in an application (i.e., in normal scarring response) that is not disclosed in either reference".

Applicant's arguments filed 12/21/07 have been fully considered but they are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the claims are drawn to a method for **"reducing the normal scarring response"** during the healing of wounds, comprising applying a furin inhibitor to a site of a

wound. The reference of Dubois teaches the method of using furin inhibitor PDX in the form of a pharmaceutical composition for the inhibition of furin or furin-like protease activity in inflammatory conditions in abnormal wound healing. The claim as recited does not imply that the method is for "reducing normal scarring". The claim as recited implies that the method is for "reducing normal scarring **response**" during the healing of **wounds**. The claim as recited does not recite "normal" or "abnormal wounds" but recites wounds in general. The reference of Pearton, et al., clearly teaches that it the elected species decanoyl-RVKR-cmk inhibits furin which is a proprotein Convertase. Since the claims are drawn to reducing normal scarring response at the wound site by application of a furin inhibitor, the combination of references cited teaches such a method.

In response to applicant's argument that "assuming that the cited references disclosed all the claimed elements of the instant claims, a person of ordinary skill in the art would find no motivation to combine the references to result in the instantly claimed invention". The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). With regards to argument that "allegedly shared cell permeability feature would not be enough to inform a person of ordinary skill in the art to use the inhibitor in an application (i.e. normal scarring response) is not disclosed in either reference", It should be noted that cell permeation of active ingredients is an important consideration in wound healing processes (Abstract of US 5874479 issued to Martin). The US 5874479 patent reference has been used to rebut the applicant's argument and it has not been used in the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as stated in the office action dated 6/22/07 and reiterated below.

Please note that the response to applicant's argument is addressed at the end of the reiterated rejection.

The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Because, in the instant application, applicants claim a method for reducing normal scarring response during the healing of wounds. The claims as recited include any and all furin inhibitors for reducing normal scarring response during healing of wounds.

The MPEP clearly states that the purpose of the written description is to ensure that the inventor had possession of invention as of the filing date of the application, of the subject matter later claimed by him. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). The

MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include, "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed invention is sufficient" MPEP 2163.

In the instant application, applicants claim a method for reducing scarring during the healing of wounds, reducing fibrosis in the treatment of fibrotic conditions, or for preventing or inhibiting scar formation or fibrosis, comprising applying a furin inhibitor to a site of a wound or fibrotic disorder or to a site where a wound may form or fibrosis may occur.

The claims as recited and as previously stated include any and all furin inhibitors. The specification lists several classes of compounds as Convertase inhibitors (page 9 of the specification) that in turn contain many species of inhibitors. The classes of compounds and species within the disclosed classes belong to different classes of biomolecules such as DNA, proteins, peptides, hormones, ribozymes, antisense DNA and organic molecules. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated: "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials.

However, in the instant case, the specification does not provide any examples or structural characteristics associated with these classes or species of inhibitors. The specification only provides the structural features of two inhibitors and they are decanoly-RVKR-cmk and hexa-arginine. The class of compounds and species within the disclosed classes belong to different classes of biomolecules such as DNA, proteins, peptides, hormones, ribozymes, antisense DNA and organic molecules. Therefore, the "furin inhibitors" as claimed in the present invention represent innumerable chemical compounds and molecules with widely varying structural characteristics. The specification is silent on the representative examples for each class of compounds in terms of structural features, chemical formulae and structure-function relations. Therefore the claims as recited and the specification as disclosed is inadequate in providing support for the invention as recited.

The claim 3 recites that the inhibitor is lipid soluble. The specification does not provide adequate description as to nature or structural features that constitute a lipid soluble molecule. Specification lacks written description to support this claim. There are innumerable numbers of molecules that are lipid soluble in literature. A peptide that comprises of only hydrophobic amino acids or a peptide modified with a lipophilic moiety is lipid soluble molecule. Any molecule attached to a polyalkyl hydrocarbon chain will also be lipid soluble molecule. The claim as recited and specification as disclosed neither provides a proper definition nor any structural characteristics associated with the inhibitor that is lipid soluble.

The claim 4 of instant application recites that the inhibitor is a peptidyl chloromethylketone having a peptide moiety that mimics at least one Convertase enzyme site. To begin with the Convertase enzyme family itself is classified according to their distribution in

various tissues and are classified into several subgroups (page 2 of Dubios reference). Mere recitation of peptidyl chloromethylketone having a peptide moiety that mimics at least one Convertase enzyme site does not provide adequate written description support to the invention without providing proper structural feature and chemical formulae that represents structure for the peptide analogs and the associated Convertase enzyme that the peptide inhibits.

The claims also recite that the method of the instant invention encompass applying furin inhibitor not only to a site of a wound or fibrotic disorder but also to a site where a wound may form or fibrosis may occur. The claim as recited implies that the furin inhibitor is applied to a site other than a site that requires the treatment implying that the furin inhibitor is applied to unknown sites on normal individuals in order to prevent the formation of scar where a wound has not formed and fibrosis has not occurred.

Therefore, the claim(s) as recited contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to applicant's arguments

Applicants argue that, "[T]he specification shows that the inventor had possession of the claimed methods at the time of filing. The pending claims are drawn to a discrete class of furin inhibitors that inhibit the activation of TGF-β. The specification includes a working example that details assays to detect inhibitors of extracellular TGF-β activation as well as showing the effectiveness of several exemplary compounds. The specification describes exemplary

compounds as well as guidance on identifying other compounds useful in the claimed methods. See the specification at pages 9-10. Moreover, the role of TGF-β in wound healing is known in the art and discussed in the specification. *Id*. Applicants further not that the claimed methods lie in the discovery that a particular class of enzymes (one of which is furin) contributes to scar formation through the activation of TGF-β. Thus, if enzymes such as furin are inhibited, less TGF-β is activated and scarring can be reduced. See, e.g., the specification at page 8-9. In sum, the specification provides sufficient detail and guidance to show that Applicants had possession of the invention at the time of filing. Nothing more is required".

Applicant's arguments filed 12/21/07 have been fully considered but they are not persuasive. Applicant's argument that the instant claims are drawn to a discrete class of furin inhibitors that inhibit the activation of TGF-β is not persuasive. Because, the TGF-β is a family of growth factors and applicants are claiming any and all furin inhibitors that inhibits this class or family of growth factors. With the exception of two inhibitors decanoyl-RVKR-cmk and hexa-arginine, the specification as disclosed is vastly silent on the nature and chemical structure of all the other classes of furin inhibitors disclosed in the specification and as stated in the rejection above.

Therefore, the claim(s) as recited contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and therefore, the rejection is appropriate and maintained.

New grounds of rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to recite that the limitation, "the normal scaring response".

Lack of Ipsis Verbis Support

The specification lacks any Ipsis Verbis support that would support the phrase "the normal scaring response". The support for the claim amendments as indicated in the remarks filed 12/21/07 at the specified locations, for e.g., at inter alia, page 8, paragraphs 1 and 2; page 12, third paragraphs. The words contained in the phrase "the normal scaring response" do not appear at the specified locations

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Lack of Implicit Support

It is acknowledged that there is it should be noted, that exact terms need not be used *in*

haec verba to satisfy the written description requirement of the first paragraph of 35 U.S.C. 112. Newly added claims or amendment can be supported by implicit, or inherent disclosure. However, the specification also lacks any implicit or inherent disclosure for the phrase "the normal scaring response". To the contrary, in the specification the word "normal" appears only at three locations, page 2, line 6 (twice) and on page 11, line 26 and the word 'normal" at these locations is not related to the phrase "the normal scaring response".

In conclusion, the specification does not provide reasonable support to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as amended.

Applicant's amendment to claim 1 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654

/Anish Gupta/
Primary Examiner, Art Unit 1654